Supplementary file 2 Talking about human papillomavirus and cancer systematic review

Background

Our previous systematic reviews of public and health professionals' views and attitudes regarding cervical cancer largely focused on HPV in the context of vaccination and cervical screening. A large number of studies had been conducted in this field and we found, in spite of the readily available information associated particularly with the public vaccination campaign, knowledge and understanding about HPV were poor. This new review was to address anal, penile and oropharyngeal cancers as well as gynaecological cancers. We anticipated that public knowledge about the HPV link to non-cervical cancers would be extremely limited. Therefore a key question for this review was how doctors should talk to patients about their HPV-related cancer diagnosis in order to help them understand the implications for their treatment choices and prognosis, whilst avoiding anxiety and distress that may result from understanding that their cancer was caused by a sexually-transmitted infection.

Methods

We used standard systematic review methods.[1] We searched the following electronic databases: Medline and Medline in Process. PsycInfo, Embase, Cinahl, Web of Knowledge (including Web of Science and BIOSIS) and The Cochrane Library (Cochrane Database of Systematic Reviews, DARE (Database of Abstracts of Reviews of Effects), the HTA Database). The following search strategy was developed for use in Medline, and adapted for the remaining databases:

1. Papillomavirus infections/
2. Human papillomavirus 16/
3. Human papillomavirus 18/
4. Human papillomavirus 31/
5. (HPV or human papillomavirus).ti,ab
6. Or 1-5

7. Uterine cervical neoplasms/
8. Anus neoplasms/
9. Penile neoplasms/
10. Vulvar neoplasms/
11. Vaginal neoplasms/
12. Exp orophayngeal neoplasms/
13. Or/ 7-12

14. Patient education/
15. Counselling/
16. ((Communicat$ or tell$ or disclos$ or advis$ or advice or educat$ or counsel$ or discuss$ or talk$ or dialog$ or discourse$ or Inform$ or reassur$ or comfort$ or support$) adj5 patient$).tw
17. ((anxi$ or worry or worri$ or concern$ or fear$ or burden$ or distress$ or alarm$) adj5 patient$).tw

18. Or/ 14-17
19. 6 and 13 and 18
20. Mass screening/
21. Condylomata acuminata/
22. (Cervical screening or Pap test or pap smear or Papanicolau$ or wart$ or condylomata acuminata).ti,ab
23. Or/ 20-22
24. 19 not 23

We also conducted forwards and backwards citation searches for included studies. Search results were managed using Endnote bibliographic software. Two reviewers screened titles and abstracts for relevance, full articles for inclusion, and appraised study quality; disagreements were resolved by discussion. We expected the literature to be sparse; therefore we considered any study of any design that shed light on these issues. We did not restrict our searches by language but, since the cancer specialists on our team estimated that relevant articles began to appear in the previous five years, we limited our searches to 2005 onwards to be certain of capturing all the relevant literature. We excluded records where only abstracts were available and non-research records such as letters and editorials. We appraised the quality of included studies using the Mixed Methods Appraisal Tool (MMAT) for mixed studies reviews[2] since this tool had the advantage of incorporating the appraisal of several different study designs (qualitative, RCT, non-RCT, observational, mixed methods) using a single tool with a coherent range of quality criteria.[3] Data were extracted into pre-defined forms include the study details; setting; population; quality score; methods; etc.

Findings

Searches conducted in November 2015 resulted in 507 records being identified after duplicates were removed. After screening abstracts and titles, 20 appeared to be relevant but on retrieval of full text articles only four studies met our inclusion criteria (Figure 1 PRISMA flow diagram). The included studies were published between 2008 and 2013 and all were conducted in the USA. All the studies were small, with samples ranging between 10 and 62 participants. In two of them the study populations comprised patients with oropharyngeal cancer. Both examined information needs and the emotional/psycho-social impacts of an HPV diagnosis; one was a quantitative study using a questionnaire supplemented by data from medical records,[4] whereas the other was a qualitative interview study.[5] In the other two studies, participants were women with CIN or cervical cancer. In the first, the quality and content of post-colposcopy consultations were investigated using audio-recordings and Likert scale responses to three questions.[6] In the final study an intervention comprising a fact sheet developed from a review of available pamphlets, appraisal by nursing staff and feedback from patients was discussed in a 40 minute consultation. A retrospective chart review was conducted comparing the intervention group with a control group to evaluate compliance to post-colposcopy recommendations.[7] Study characteristics are outlined in table 1.

Two studies reported significant knowledge gaps among patients;[4 5] one specifically identified uncertainty about HPV transmission, latency and communicability and also noted that patients found information scarce and not easily navigated on the internet.[5] Three of the studies reported moderate levels of worry or distress among patients,[4-6] though one of them noted relatively low levels of self-blame.[4] The studies concluded that patient information increased compliance to

treatment,[7] but HPV was rarely discussed in consultations,[6] and additional resources giving information in a consistent way,[5] and research to establish best practice guidelines are needed.[4]

Study quality was somewhat variable and difficult to assess because of omissions in reporting. The qualitative study appeared to be well-conducted but consideration of the study context and researcher influence were not reported. Also they were not able to recruit any female participants with oropharyngeal cancer, who may have had different responses to the male participants.[5] Of the two quantitative descriptive studies, one appeared to be well-conducted and well-reported but unfortunately had a low response rate of only 41%.[4] The other investigated a sub-sample of women enrolled in a wider study and did not report either the method of recruitment or the response rate, so it was not possible to tell whether the sample was representative.[6] Finally the quantitative non-randomised study recruited a small, convenience sample. It was not clear whether there might have been differences between the intervention and control groups because of the different methods of recruiting them; also the response rate was not reported.[7]

Discussion

The four included studies, two of oropharyngeal cancer and two of cervical cancer reported knowledge gaps, information needs, and worry and distress about HPV. Despite comprehensive searches, the relevant literature was sparse. There were no studies relating to anal, penile, vulvar or vaginal cancers. All the studies took place in the USA so we cannot say whether their findings are likely to be transferrable to other countries or settings. The studies were small and of only moderate quality. Nevertheless, the findings of the studies were consistent with each other and with other literature, in relation to cervical cancer at least,[8-10] and so are likely to be reliable. We could not draw any new conclusions but the findings supported the development of new messages to contribute to the content of evidence-based, cancer site-specific scripted consultations, which was the purpose of this review.

Figure 1: PRISMA 2009 Flow Diagram

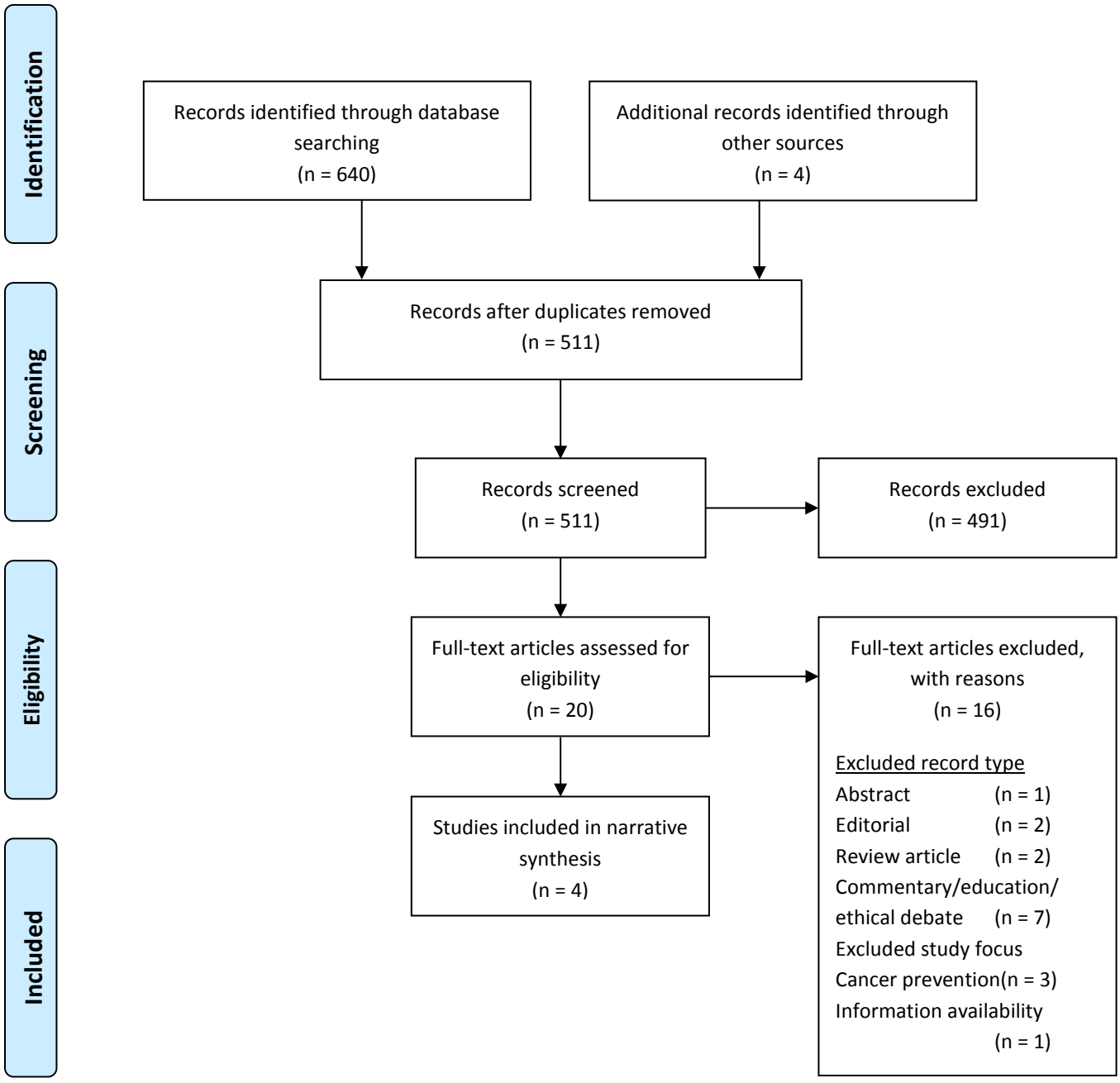

Table 1 Characteristics of included studies

Study, location, setting	**Data collection methods**	**Participant details**	**Analysis method**	**Study focus** **questions asked**
Milbury, 2013 USA Texas A comprehensive cancer care centre	Paper-and-pencil questionnaire with closed and open questions; data from electronic medical records	62 patients, partnered ≥ 1 year, beginning radiotherapy for HPV+ oropharyngeal cancer Mean age 60 years 53 male 57 White 47 > high school degree 7 never smoked	Statistical analysis using SPSS v19 Responses to open-ended questions were tabulated, categorised and reported in summary fashion	Informational and psycho-social needs Cancer cause Secrecy/disclosure/discussion of HPV with partner; partner's risk of HPV and cancer Impact of HPV on relationship with partner How informed they felt, information needs and sources Level of cancer distress and cancer blame Demographic information Cancer related medical variables
Baxi, 2013 USA New York A National Cancer Institute-designated cancer centre	Semi-structured interviews with open-ended questions	10 White, male patients with HPV+ oropharyngeal cancer 1-5 years from treatment completion Mean age 57 years (range 42-63) 8 partnered; 2 single All were employed 7 never smoked 7 drank <1 alcoholic drink per day	Thematic analysis using the 4 domains of the topic guide as a framework for the analysis Responses to the multiple choice questions were summed and tabulated	Emotional impact of HPV and information needs *Questions in 4 domains:* Communication about HPV Knowledge about HPV Psychological reaction to a diagnosis of HPV Sexual impact of being diagnosed with HPV *2 multiple choice questions:* Information sources about HPV Emotional reactions to HPV diagnosis
Pruitt, 2008 USA	Audio-recorded consultations with 11 healthcare professionals, and 3 questions asked by	47 women 2-3 weeks after colposcopy examination and biopsy	Deductive content analysis using ATLAS.ti and SPSS v14	Content and quality of post-colposcopy consultations Content of consultations plus 3 questions to women:

Texas A public county hospital, a Gynae oncology clinic in a cancer centre and university-affiliated Gynae clinic	the researcher after the consultation	Age 18-69 years; 23 ≤ 29 years 21 White Hispanic 16 Black non-Hispanic 8 White non-Hispanic 21 CIN 1; 15 CIN 2-3; 2 cancer	Use of quallitative and quantitative software to provide qualitative description of communication content and comparison of the content by diagnosis	*On a scale of 1-10* How well did the healthcare provider explain your test results? How serious do you think your health problem is? How worried are you about your health problem?
Olbrys, 2011 USA New York A community gynaecology clinic	Retrospective chart review to collect data on demographics, pap test and biopsy results, treatment recommendations and subsequent appointment attendance	60 women referred for colposcopy 30 received an educational intervention; 30 controls. Age 19-62 years 46 White non-Hispanic 6 Black non-Hispanic 6 White Hispanic; 2 other 19 had no health insurance 21 mild/moderate dysplasia 5 high grade dysplasia 1 endometrial cancer 3 other	Control group interrupted time series design using SPSS. Comparison between the intervention group, who reviewed the fact sheet in a 40-minute consultation with a nurse practitioner colposcopist, and the control group who did not. Evaluation of compliance to post-colposcopy recommendations. Comparison of no-show rates.	<u>Fact sheets, developed by review of available pamphlets, appraisal by nursing staff and feedback from patients, discussed in a 40 minute consultation (intervention)</u> *Discussion included:* Risk factors for HPV infection Subsequent risk for cervical cancer Immune system response Association between smoking and cervical cancer Pap smear results and colposcopy procedure, risks and benefits.

Table 2 Quality appraisal

Types of study	Methodological quality criteria	Yes	No	Can't tell	comments
Screening questions	Are there clear qualitative and quantitative research questions (or objectives), or a clear mixed methods question (or objective)?	✓			

(for all types)	Do the collected data allow address the research question (objective)? E.g., consider whether the follow-up period is long enough for the outcome to occur (for longitudinal studies or study components).	✓			
	Further appraisal may be not feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				
1. Qualitative	1.1. Are the sources of qualitative data (archives, documents, informants, observations) relevant to address the research question (objective)?				
	1.2. Is the process for analyzing qualitative data relevant to address the research question (objective)?				
	1.3. Is appropriate consideration given to how findings relate to the context, e.g., the setting, in which the data were collected?				
	1.4. Is appropriate consideration given to how findings relate to researchers' influence, e.g., through their interactions with participants?				
2. Quantitative randomised controlled (trials)	2.1. Is there a clear description of the randomization (or an appropriate sequence generation)?				
	2.2. Is there a clear description of the allocation concealment (or blinding when applicable)?				
	2.3. Are there complete outcome data (80% or above)?				
	2.4. Is there low withdrawal/drop-out (below 20%)?				
3. Quantitative nonrandomized **Milbury, 2013**	3.1. Are participants (organizations) recruited in a way that minimizes selection bias?	✓			All consecutive eligible patients
	3.2. Are measurements appropriate (clear origin, or validity known, or standard instrument; and absence of contamination between groups when appropriate) regarding the exposure/intervention and outcomes?	✓			
	3.3. In the groups being compared (exposed vs. non-exposed; with intervention vs. without; cases vs. controls), are the participants comparable, or do researchers take into account (control for) the difference between these groups?	✓			
	3.4. Are there complete outcome data (80% or above), and, when applicable, an acceptable response rate (60% or above), or an acceptable follow-up rate for cohort studies (depending on the duration of follow-up)?			✓	41%
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the quantitative research question (quantitative aspect of the mixed methods question)?				
	4.2. Is the sample representative of the population understudy?				

	4.3. Are measurements appropriate (clear origin, or validity known, or standard instrument)?				
	4.4. Is there an acceptable response rate (60% or above)?				
5. Mixed methods	5.1. Is the mixed methods research design relevant to address the qualitative and quantitative research questions (or objectives), or the qualitative and quantitative aspects of the mixed methods question (or objective)?				
	5.2. Is the integration of qualitative and quantitative data (or results*) relevant to address the research question (objective)?				
	5.3. Is appropriate consideration given to the limitations associated with this integration, e.g., the divergence of qualitative and quantitative data (or results*) in a triangulation design?				

Types of study	**Methodological quality criteria**	**Yes**	**No**	**Can't tell**	**comments**
Screening questions **(for all types)**	Are there clear qualitative and quantitative research questions (or objectives), or a clear mixed methods question (or objective)?	✓			
	Do the collected data allow address the research question (objective)? E.g., consider whether the follow-up period is long enough for the outcome to occur (for longitudinal studies or study components).	✓			
	Further appraisal may be not feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				
1. Qualitative **Baxi 2013**	1.1. Are the sources of qualitative data (archives, documents, informants, observations) relevant to address the research question (objective)?	✓			Only men were recruited
	1.2. Is the process for analyzing qualitative data relevant to address the research question (objective)?	✓			
	1.3. Is appropriate consideration given to how findings relate to the context, e.g., the setting, in which the data were collected?			✓	Not reported
	1.4. Is appropriate consideration given to how findings relate to researchers' influence, e.g., through their interactions with participants?			✓	Not reported

2. Quantitative randomised controlled (trials)	2.1. Is there a clear description of the randomization (or an appropriate sequence generation)?				
	2.2. Is there a clear description of the allocation concealment (or blinding when applicable)?				
	2.3. Are there complete outcome data (80% or above)?				
	2.4. Is there low withdrawal/drop-out (below 20%)?				
3. Quantitative nonrandomized	3.1. Are participants (organizations) recruited in a way that minimizes selection bias?				
	3.2. Are measurements appropriate (clear origin, or validity known, or standard instrument; and absence of contamination between groups when appropriate) regarding the exposure/intervention and outcomes?				
	3.3. In the groups being compared (exposed vs. non-exposed; with intervention vs. without; cases vs. controls), are the participants comparable, or do researchers take into account (control for) the difference between these groups?				
	3.4. Are there complete outcome data (80% or above), and, when applicable, an acceptable response rate (60% or above), or an acceptable follow-up rate for cohort studies (depending on the duration of follow-up)?				
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the quantitative research question (quantitative aspect of the mixed methods question)?				
	4.2. Is the sample representative of the population understudy?				
	4.3. Are measurements appropriate (clear origin, or validity known, or standard instrument)?				
	4.4. Is there an acceptable response rate (60% or above)?				
5. Mixed methods	5.1. Is the mixed methods research design relevant to address the qualitative and quantitative research questions (or objectives), or the qualitative and quantitative aspects of the mixed methods question (or objective)?				
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Types of study	Methodological quality criteria	Yes	No	Can't tell	comments
Screening questions **(for all types)**	Are there clear qualitative and quantitative research questions (or objectives), or a clear mixed methods question (or objective)?	✓			
	Do the collected data allow address the research question (objective)? E.g., consider whether the follow-up period is long enough for the outcome to occur (for longitudinal studies or study components).	✓			
	Further appraisal may be not feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				
1. Qualitative	1.1. Are the sources of qualitative data (archives, documents, informants, observations) relevant to address the research question (objective)?				
	1.2. Is the process for analyzing qualitative data relevant to address the research question (objective)?				
	1.3. Is appropriate consideration given to how findings relate to the context, e.g., the setting, in which the data were collected?				
	1.4. Is appropriate consideration given to how findings relate to researchers' influence, e.g., through their interactions with participants?				
2. Quantitative randomised controlled (trials)	2.1. Is there a clear description of the randomization (or an appropriate sequence generation)?				
	2.2. Is there a clear description of the allocation concealment (or blinding when applicable)?				
	2.3. Are there complete outcome data (80% or above)?				
	2.4. Is there low withdrawal/drop-out (below 20%)?				
3. Quantitative nonrandomized	3.1. Are participants (organizations) recruited in a way that minimizes selection bias?				
	3.2. Are measurements appropriate (clear origin, or validity known, or standard instrument; and absence of contamination between groups when appropriate) regarding the exposure/intervention and outcomes?				

	3.3. In the groups being compared (exposed vs. non-exposed; with intervention vs. without; cases vs. controls), are the participants comparable, or do researchers take into account (control for) the difference between these groups?				
	3.4. Are there complete outcome data (80% or above), and, when applicable, an acceptable response rate (60% or above), or an acceptable follow-up rate for cohort studies (depending on the duration of follow-up)?				
4. Quantitative descriptive **Pruitt 2008**	4.1. Is the sampling strategy relevant to address the quantitative research question (quantitative aspect of the mixed methods question)?	✓			
	4.2. Is the sample representative of the population understudy?			✓	A subset of women enrolled in another study, recruitment methods not reported
	4.3. Are measurements appropriate (clear origin, or validity known, or standard instrument)?	✓			Questions described; coding for consultations available from the authors
	4.4. Is there an acceptable response rate (60% or above)?			✓	A subset of women enrolled in another study, response rate not reported
5. Mixed methods	5.1. Is the mixed methods research design relevant to address the qualitative and quantitative research questions (or objectives), or the qualitative and quantitative aspects of the mixed methods question (or objective)?				
	5.2. Is the integration of qualitative and quantitative data (or results*) relevant to address the research question (objective)?				
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Screening questions **(for all types)**	Are there clear qualitative and quantitative research questions (or objectives), or a clear mixed methods question (or objective)?	✓			
	Do the collected data allow address the research question (objective)? E.g., consider whether the follow-up period is long enough for the outcome to occur (for longitudinal studies or study components).	✓			
	Further appraisal may be not feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				

1. Qualitative	1.1. Are the sources of qualitative data (archives, documents, informants, observations) relevant to address the research question (objective)?				
	1.2. Is the process for analyzing qualitative data relevant to address the research question (objective)?				
	1.3. Is appropriate consideration given to how findings relate to the context, e.g., the setting, in which the data were collected?				
	1.4. Is appropriate consideration given to how findings relate to researchers' influence, e.g., through their interactions with participants?				
2. Quantitative randomised controlled (trials)	2.1. Is there a clear description of the randomization (or an appropriate sequence generation)?				
	2.2. Is there a clear description of the allocation concealment (or blinding when applicable)?				
	2.3. Are there complete outcome data (80% or above)?				
	2.4. Is there low withdrawal/drop-out (below 20%)?				
3. Quantitative nonrandomized **Olbrys 2011**	3.1. Are participants (organizations) recruited in a way that minimizes selection bias?			✓	Convenience sample
	3.2. Are measurements appropriate (clear origin, or validity known, or standard instrument; and absence of contamination between groups when appropriate) regarding the exposure/intervention and outcomes?	✓			
	3.3. In the groups being compared (exposed vs. non-exposed; with intervention vs. without; cases vs. controls), are the participants comparable, or do researchers take into account (control for) the difference between these groups?			✓	Control group were recruited in a different way so not clear whether the 2 groups were similar
	3.4. Are there complete outcome data (80% or above), and, when applicable, an acceptable response rate (60% or above), or an acceptable follow-up rate for cohort studies (depending on the duration of follow-up)?			✓	Response rate not reported
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the quantitative research question (quantitative aspect of the mixed methods question)?				
	4.2. Is the sample representative of the population understudy?				
	4.3. Are measurements appropriate (clear origin, or validity known, or standard instrument)?				
	4.4. Is there an acceptable response rate (60% or above)?				

5. Mixed methods	5.1. Is the mixed methods research design relevant to address the qualitative and quantitative research questions (or objectives), or the qualitative and quantitative aspects of the mixed methods question (or objective)?				
	5.2. Is the integration of qualitative and quantitative data (or results*) relevant to address the research question (objective)?				
	5.3. Is appropriate consideration given to the limitations associated with this integration, e.g., the divergence of qualitative and quantitative data (or results*) in a triangulation design?				

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